Phase 3 Clinical Trials: Latest Updates

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Asia-Pacific Vitreo-retina Society Congress | Gold Coast, Australia

The following presentation discusses OTX-TKI, an investigational product candidate that has not been approved by the FDA or any other regulatory body; safety and effectiveness have not been established

OCULAR THERAPEUTIX

Retina experience redefined

SOL: OTX-TKI Phase 3 Clinical Program in nAMD

Evaluating the efficacy, durability and safety of OTX-TKI in nAMD

Registrational Trials

SOL-1

Phase 3
Superiority Trial

Durability of a single OTX-TKI injection

SOL-R

Phase 3
Non-Inferiority Trial

Repeat dosing every 6 months

Complementary studies designed to provide a comprehensive characterization of OTX-TKI across patient populations

Extension Study

SOL-X

Open-Label Extension

Long-term safety and disease modifying potential of continuous VEGF suppression

Eligible patients who complete end of Year 2 visit in SOL-1 or SOL-R

OCULAR THERAPEUTIX Retina experience redefined

ClinicalTrials.gov identifier: NCT06223958
ClinicalTrials.gov identifier: NCT06495918
ClinicalTrials.gov identifier: NCT07516132
nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

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Study Design: OTX-TKI and Aflibercept Direct Comparison

SOL-1

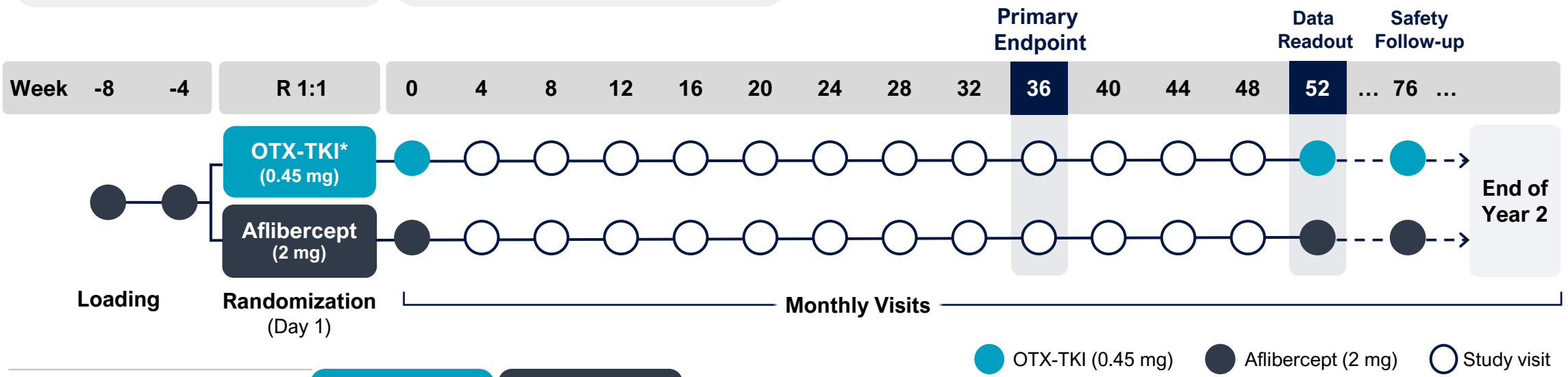
Key Enrollment Criteria (Screening)

- Treatment naïve
- **BCVA ≥54 ETDRS letters** (~20/80)
- **CSFT of ≤500 µm**

Key Randomization Criteria (Day 1)

- **BCVA gain ≥10 ETDRS letters**
  OR
  BCVA ≥84 ETDRS letters (~20/20)
- **CSFT of ≤350 µm**

Proportion of subjects who maintained visual acuity, defined as <15 ETDRS letters of BCVA loss from baseline at Week 36



Baseline (Randomization) Study Eye Characteristics	OTX-TKI 0.45 mg N = 172†	Aflibercept 2 mg N = 172
Mean (SD) BCVA, ETDRS letter score, Snellen Equivalent	80.8 (7.6) ~20/25	79.2 (7.9) ~20/25
Mean (SD) CSFT, µm,	219.3 (37.1)	226.8 (42.1)

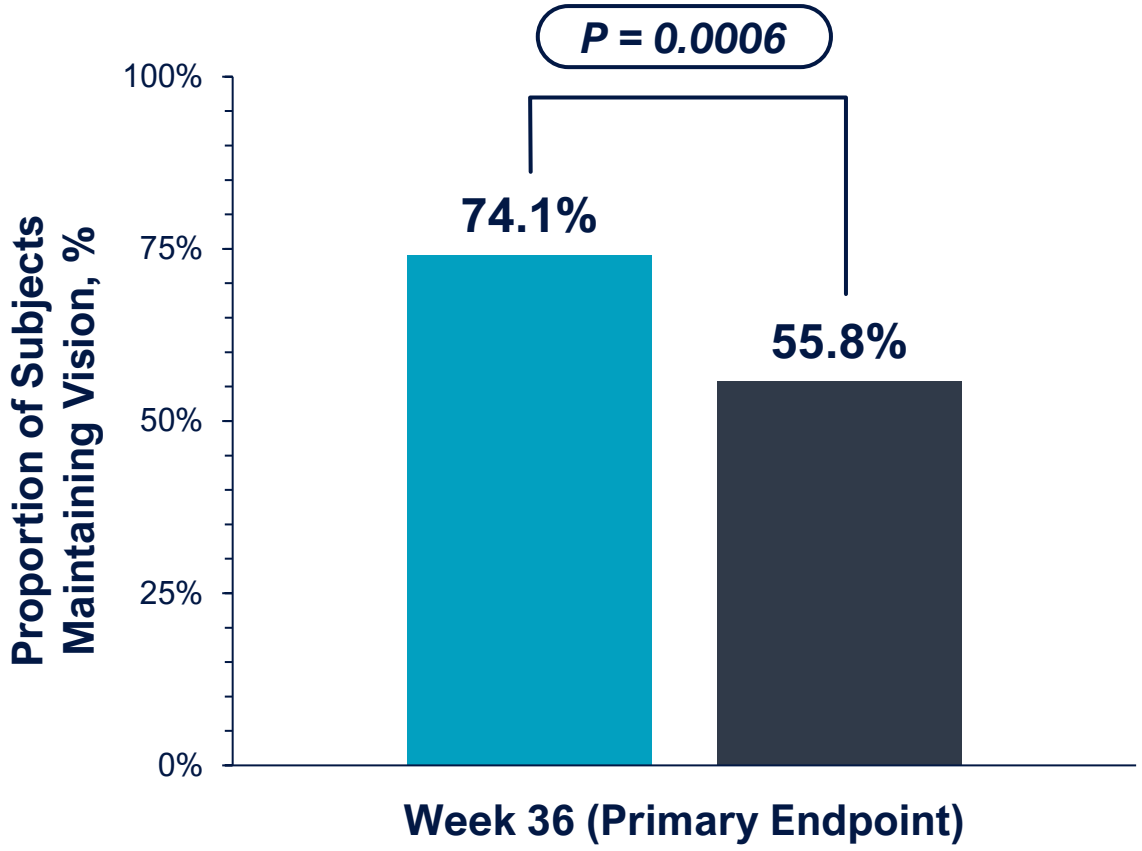
OCULAR THERAPEUTIX Retina experience redefined

*No aflibercept injection is given at baseline;
†Two OTX-TKI subjects were misrandomized, did not receive study treatment and were not included in the full analysis set
ClinicalTrials.gov. identifier: NCT06223958
Rescue Criteria: BCVA loss ≥15 ETDRS letters from baseline due to nAMD; or New macular hemorrhage that would likely lead to irreversible vision loss if left untreated in the opinion of the investigator after discussion with Medical Monitor
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation

OTX-TKI Successfully Met Superiority Primary Endpoint

SOL-1

Vision Maintenance* with a Single Injection of OTX-TKI at Week 36



18.3%
Observed difference

Clear benefit† with OTX-TKI vs Aflibercept 2 mg

0.0006
P value

High statistical significance bolsters confidence in results

- OTX-TKI 0.45 mg (n=170)
- Aflibercept 2 mg (n=172)

OCULAR THERAPEUTIX Retina experience redefined™

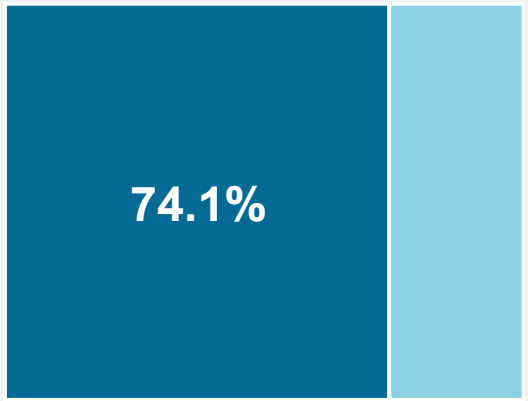
At Week 52, the proportion of subjects maintaining visual acuity* was 65.9% in the OTX-TKI arm and 44.2% in the aflibercept 2mg arm (P<0.0001)
*Vision maintenance defined as <15 ETDRS letters of loss.
† 18.3% observed difference of vision maintainers at Week 36 in OTX-TKI vs Aflibercept arm, 17.5% risk difference
ETDRS, early treatment diabetic retinopathy

OTX-TKI Demonstrated Strong Potential for Annual Dosing

Superiority Primary Endpoint Successfully Met: OTX-TKI Demonstrated Superior Maintenance of Vision*

Month 9 Results

~3 of 4 OTX-TKI subjects maintained vision* with a single injection



P = 0.0006

*Maintained vision defined as <15 ETDRS letters of loss.
ETDRS, early treatment diabetic retinopathy study

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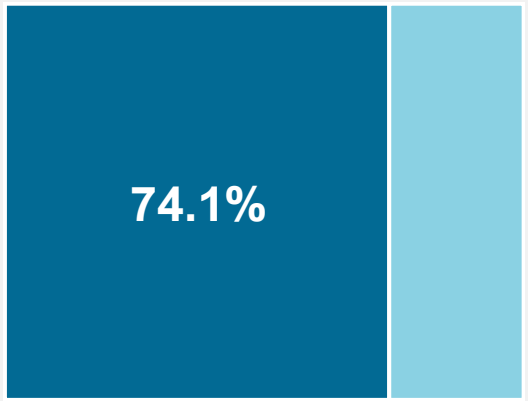
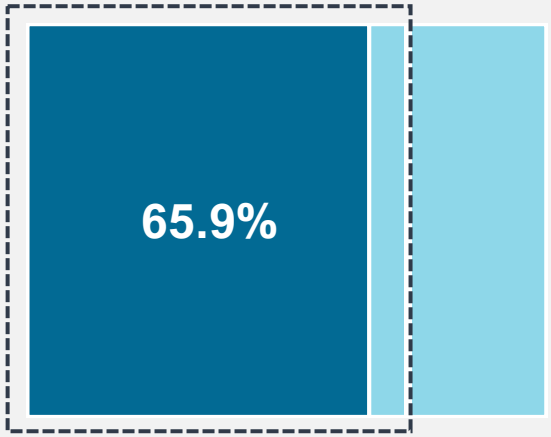


P = 0.0006

Month 12 Results

~2 of 3 OTX-TKI subjects maintained vision* with a single injection



P < 0.0001

Unmatched Durability Observed with OTX-TKI in SOL-1

OCULAR THERAPEUTIX Retina experience redefined™

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ETDRS, early treatment diabetic retinopathy study

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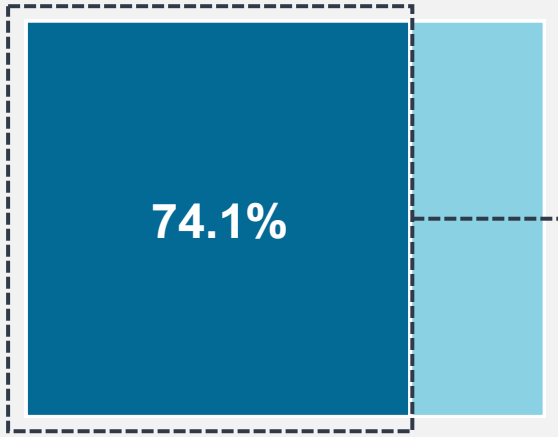

***P* = 0.0006**

Month 12 Results

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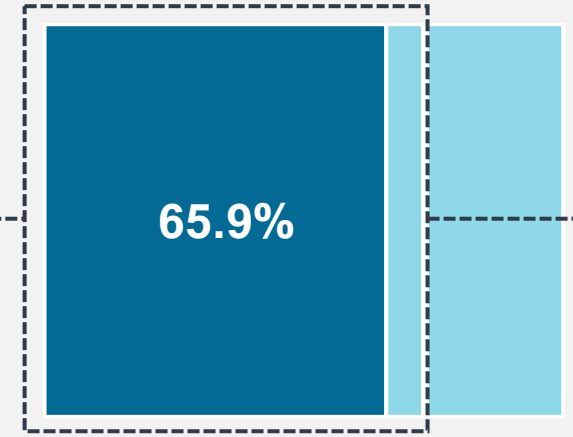
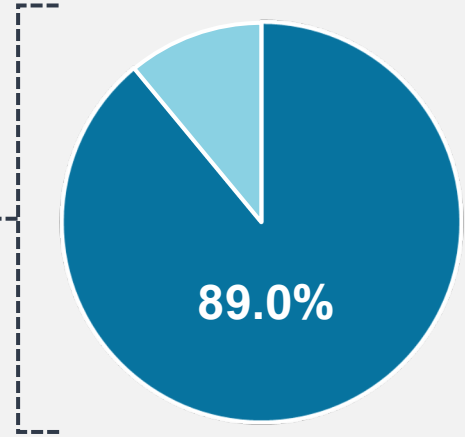


***P* < 0.0001**

Continued Response

Of subjects that maintained vision at Month 9, **~90%** maintained vision **at Month 12**

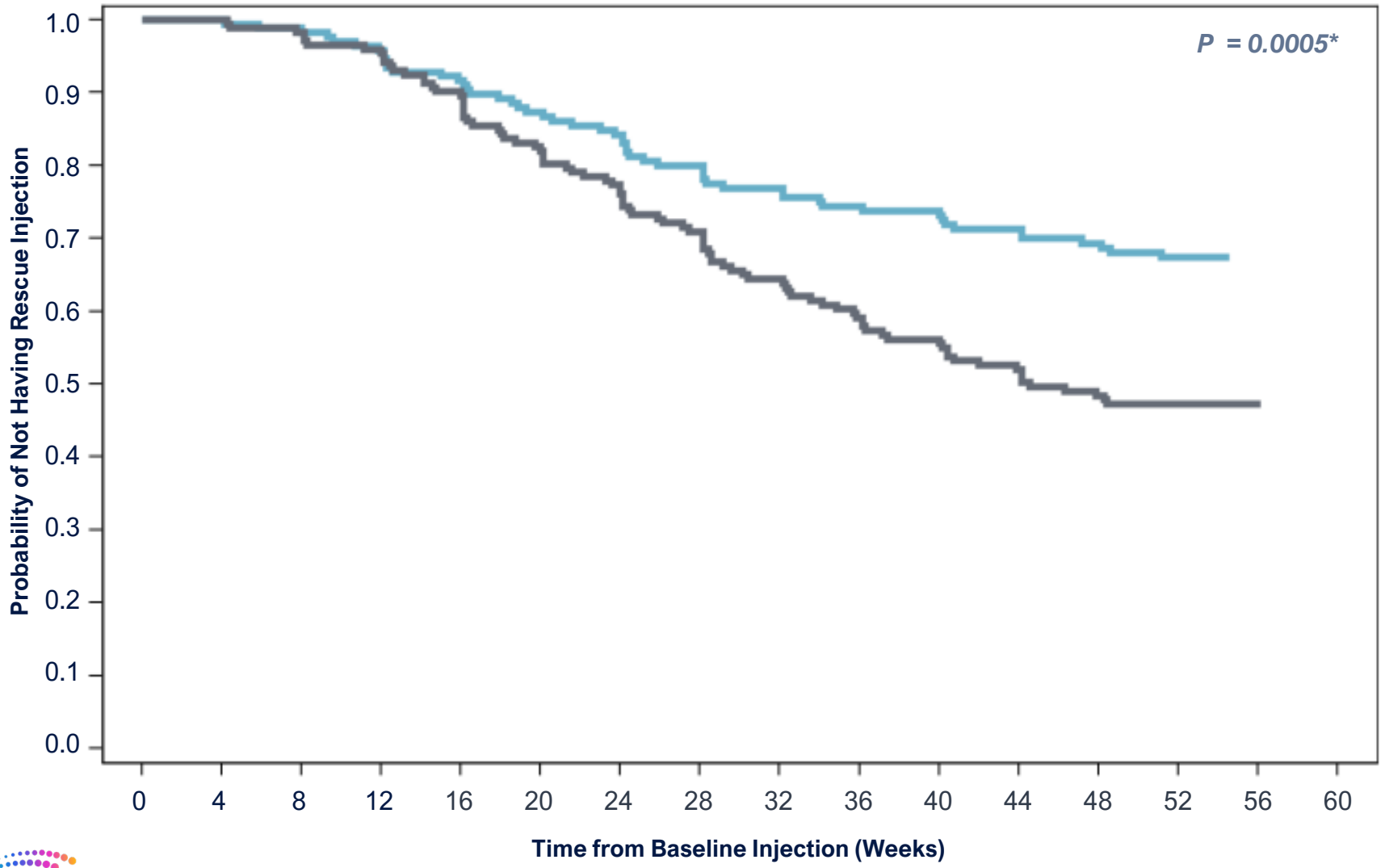


Unmatched Durability Observed with OTX-TKI in SOL-1

OCULAR THERAPEUTIX Retina experience redefined™

*Maintained vision defined as <15 ETDRS letters of loss.
ETDRS, early treatment diabetic retinopathy study

Significantly Lower Risk of Rescue During Year 1 with OTX-TKI



Secondary Endpoint: Time to First Rescue Treatment

OTX-TKI 0.45 mg (n=170)
Aflibercept 2 mg (n=172)

Rescue-free subjects include those who did not require rescue injections as specified by the protocol
*Nominal P value

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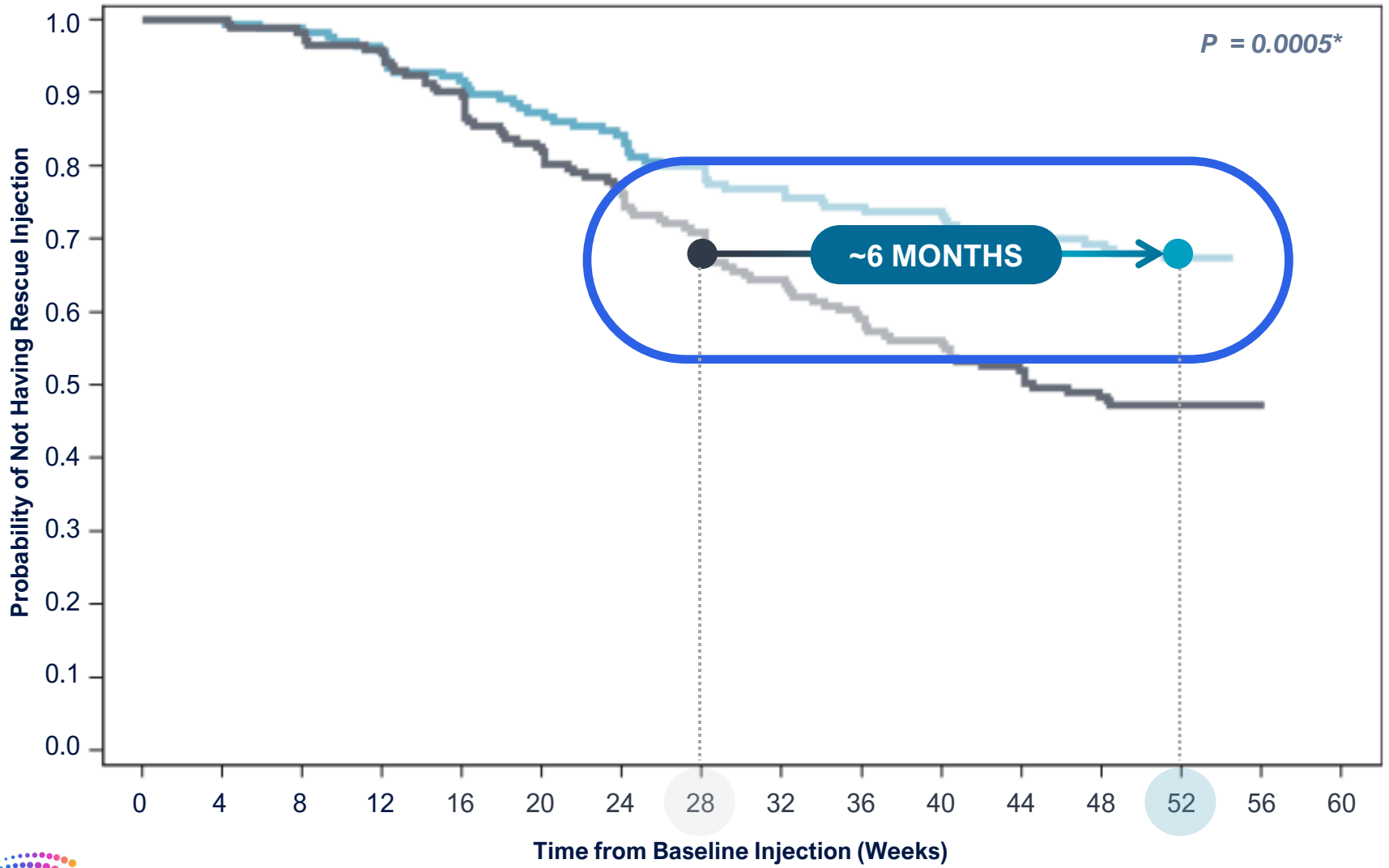


Secondary Endpoint: Time to First Rescue Treatment

~6 Month Difference

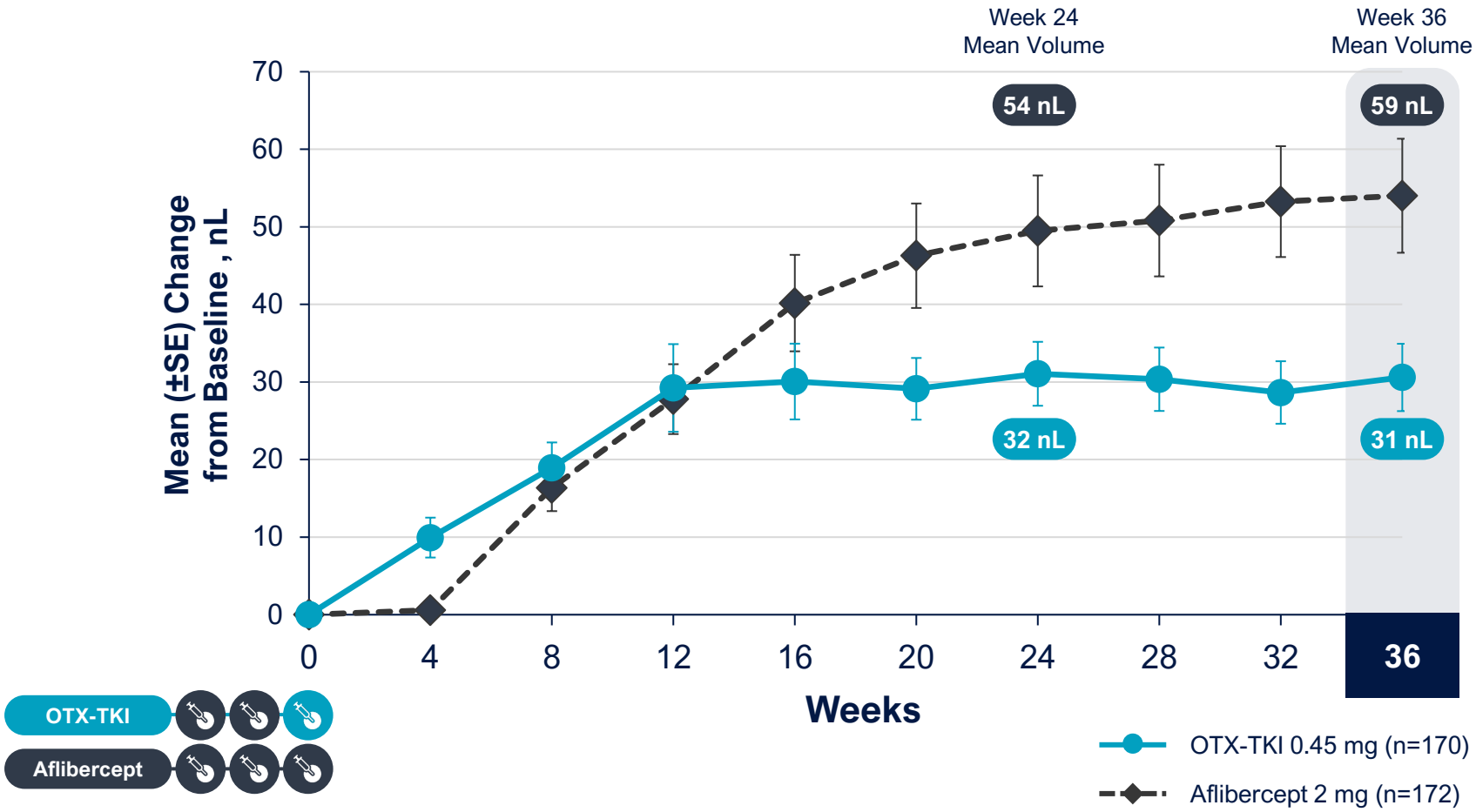
OTX-TKI Week 52 rescue rate reflects ***~6-month*** **advantage** over aflibercept

OTX-TKI 0.45 mg (n=170)
Aflibercept 2 mg (n=172)

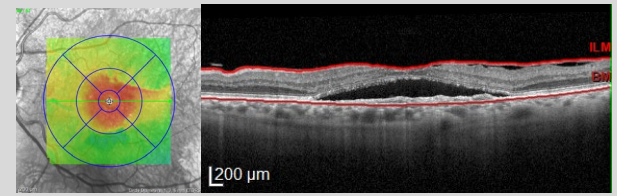
Rescue-free subjects include those who did not require rescue injections as specified by the protocol
*Nominal P value
AMD, age-related macular degeneration

OTX-TKI Delivered Sustained Fluid Control

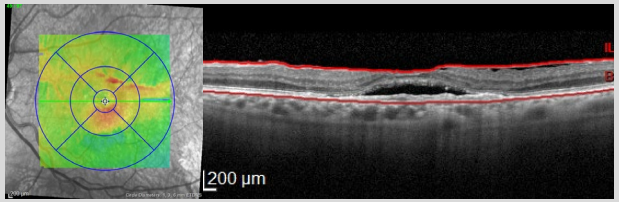
Prespecified Exploratory Analysis: Mean Change in Intra-Retinal and Sub-Retinal Fluid Volume



Total Fluid Volume: 60 nL



Total Fluid Volume: 30 nL

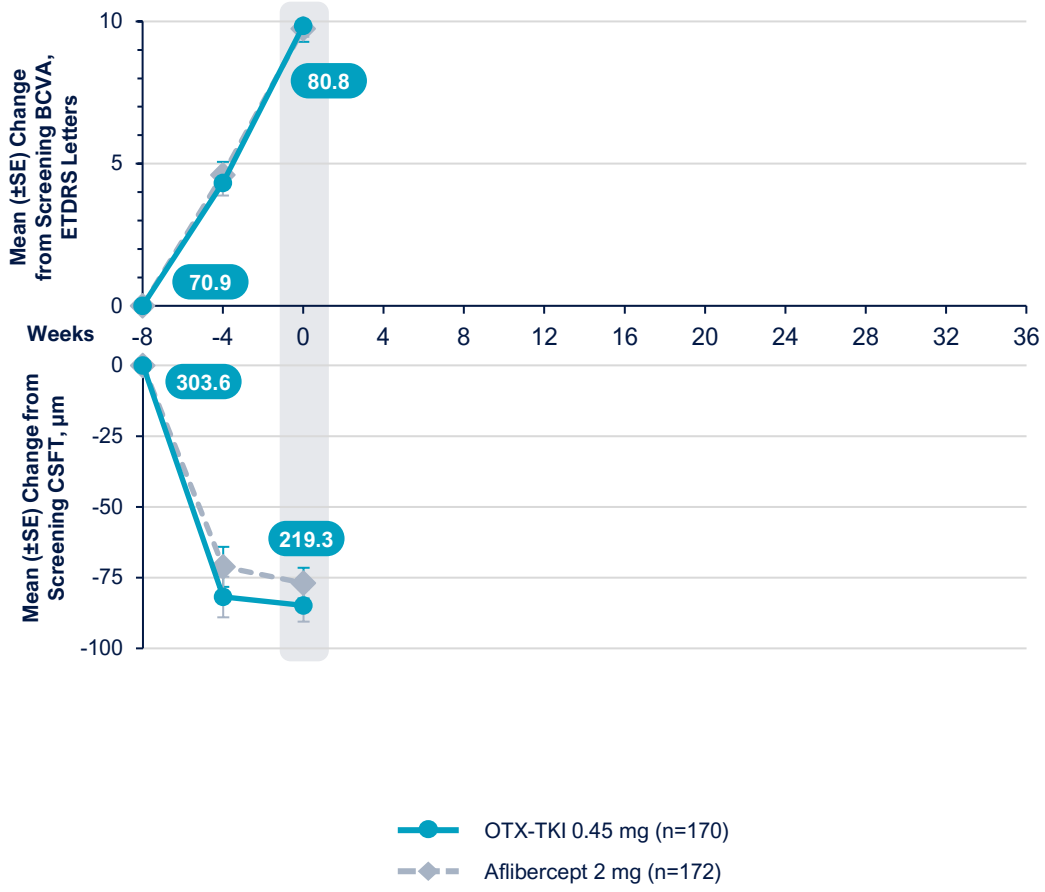


OCULAR THERAPEUTIX Retina experience redefined

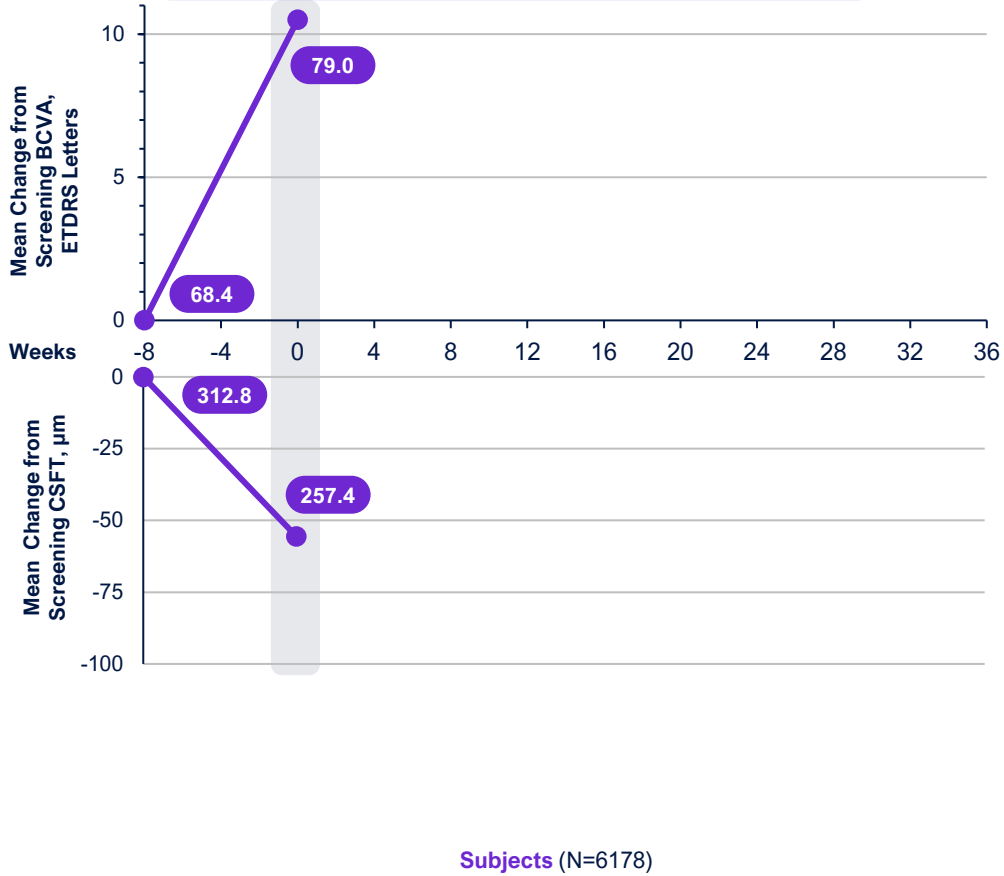
Full analysis set
SE, standard error

How Does SOL-1 Data Align with Real World Outcomes?

SOL-1 Clinical Trial
Post Hoc Analysis



SOL-1 Emulated Population
IRIS Registry



Subjects (N=6178)

OCULAR THERAPEUTIX Retina experience redefined™

Data on File 046. Ocular Therapeutix. 2026

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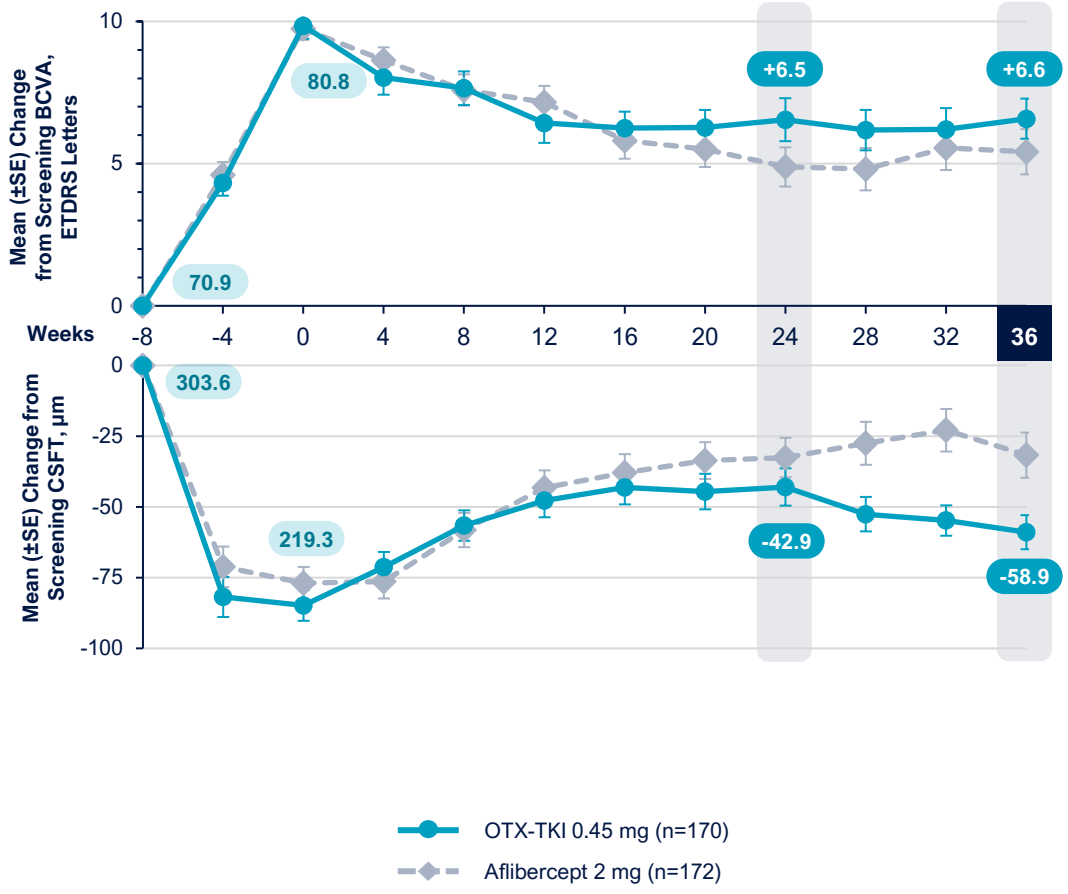

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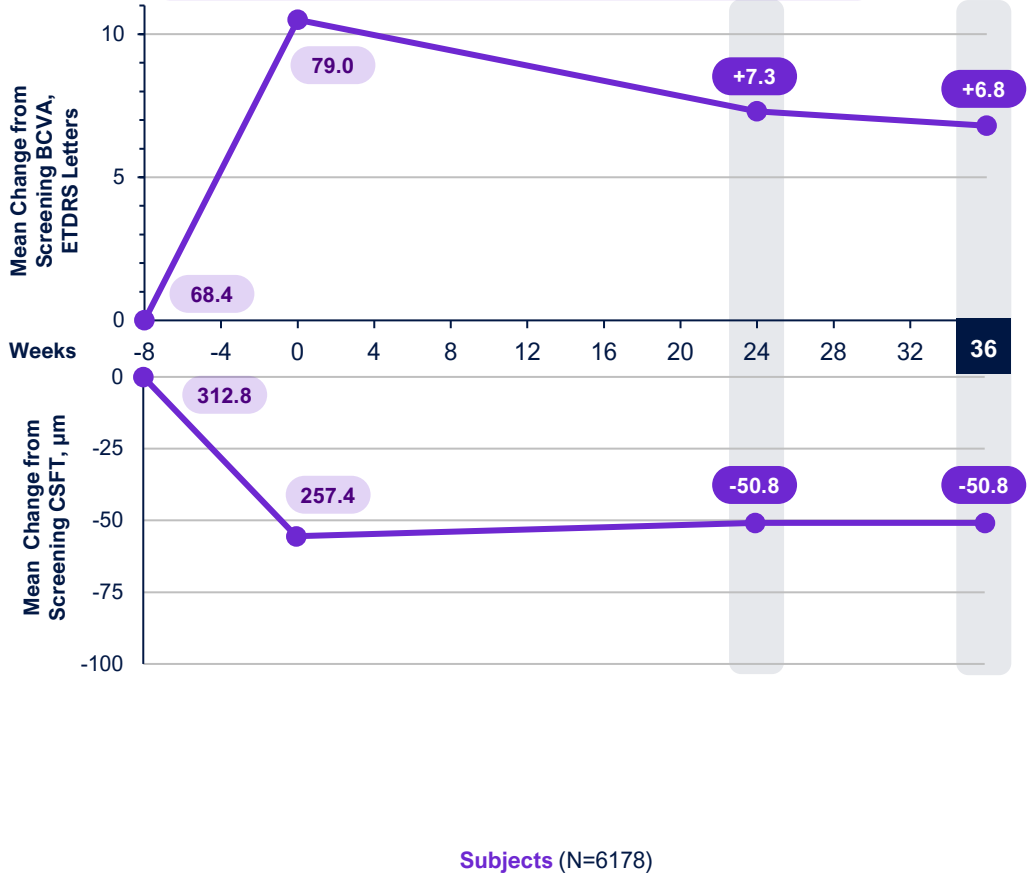

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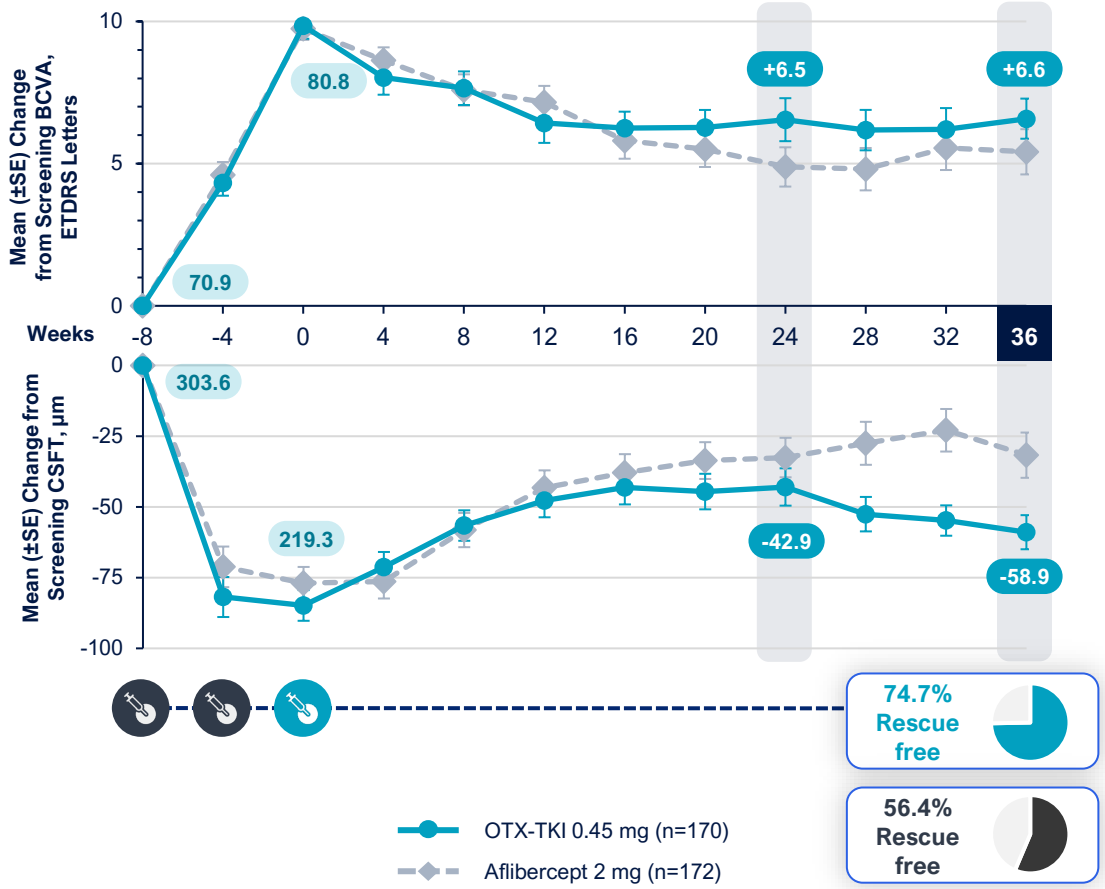

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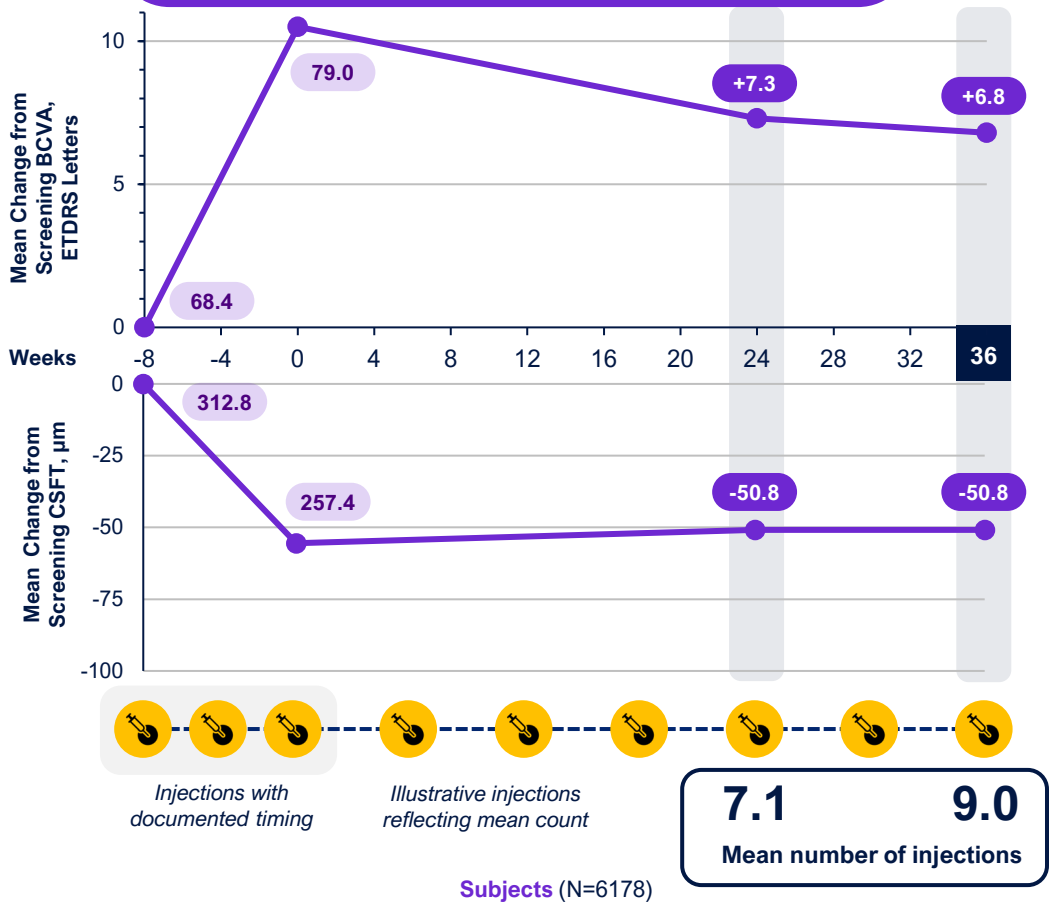


Data on File 046. Ocular Therapeutix. 2026

OTX-TKI was Generally Well Tolerated

Ocular Adverse Events in the Study Eye

Subjects with Ocular AEs (> 2%) Through Week 52, n (%)	OTX-TKI 0.45 mg n = 170	Aflibercept 2 mg n = 172
Vitreous floaters	21 (12.4)	2 (1.2)
Cataract	12 (7.1)	5 (2.9)
Conjunctival hemorrhage	11 (6.5)	5 (2.9)
Retinal hemorrhage	10 (5.9)	17 (9.9)
Dry eye	7 (4.1)	2 (1.2)
Vitreous detachment	7 (4.1)	3 (1.7)
Punctate keratitis	6 (3.5)	0
Vitreous opacities	6 (3.5)	0
Eye pain	5 (2.9)	1 (0.6)
Anterior chamber opacity	4 (2.4)	0
Posterior capsule opacification	4 (2.4)	6 (3.5)

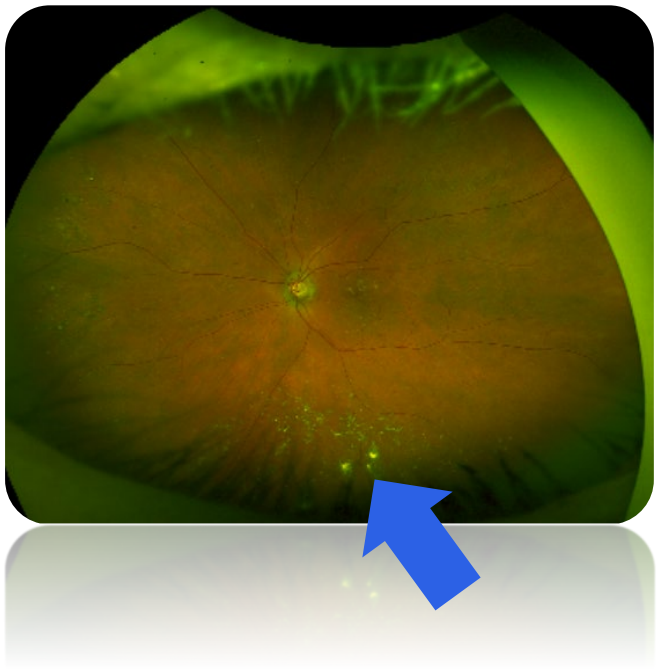
- Nine IOI events observed in study eyes of 7 subjects in the OTX-TKI arm
  - All cases were mild or moderate in severity and resolved
- **There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis**

AE, adverse event; IOI, intraocular inflammation

Appearance of Floaters May Correspond to Hydrogel Dissolution and Drug Elution

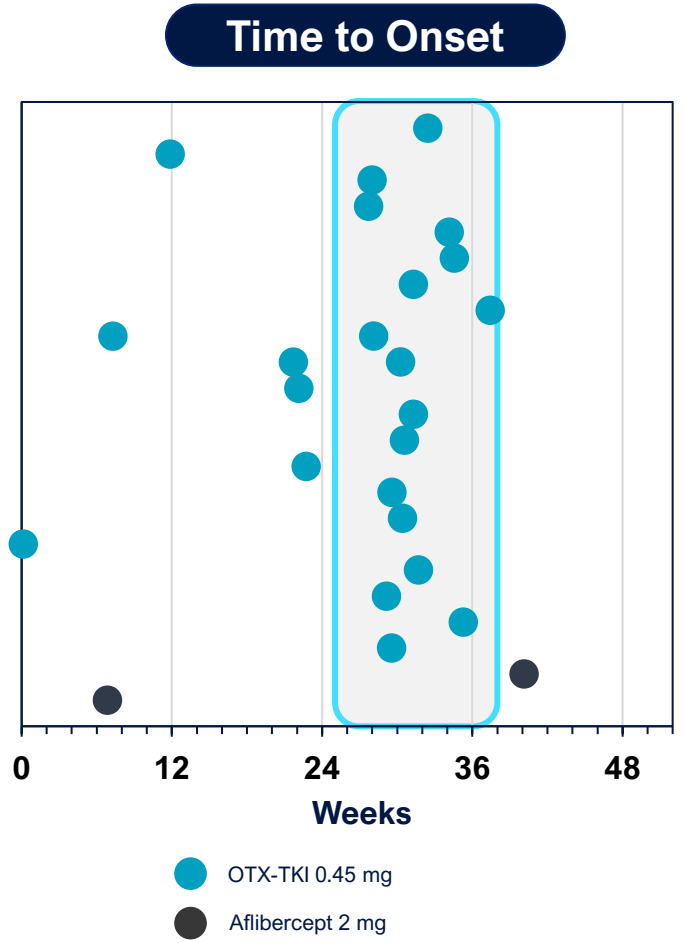
SOL-1

Evaluation of Vitreous Floaters



	OTX-TKI 0.45 mg n = 23*	Aflibercept 2 mg n = 2
Time to onset, days		
Mean (SD)	187.9 (64.0)	164.5 (164.8)
Median	207.0	164.5
BCVA change from prior visit before onset of floaters, ETDRS letters		
Mean change (SD)	-0.4 (5.0)	-5.5 (6.4)
Median change	0.0	-5.5

- All cases were mild to moderate in severity
- No evidence of IOI associated with floaters
- Onset of vitreous floaters AE coincides with drug elution stage of OTX-TKI hydrogel bioresorption process
- **For all subjects** with vitreous floaters AE reported, **drug particles are no longer visible**



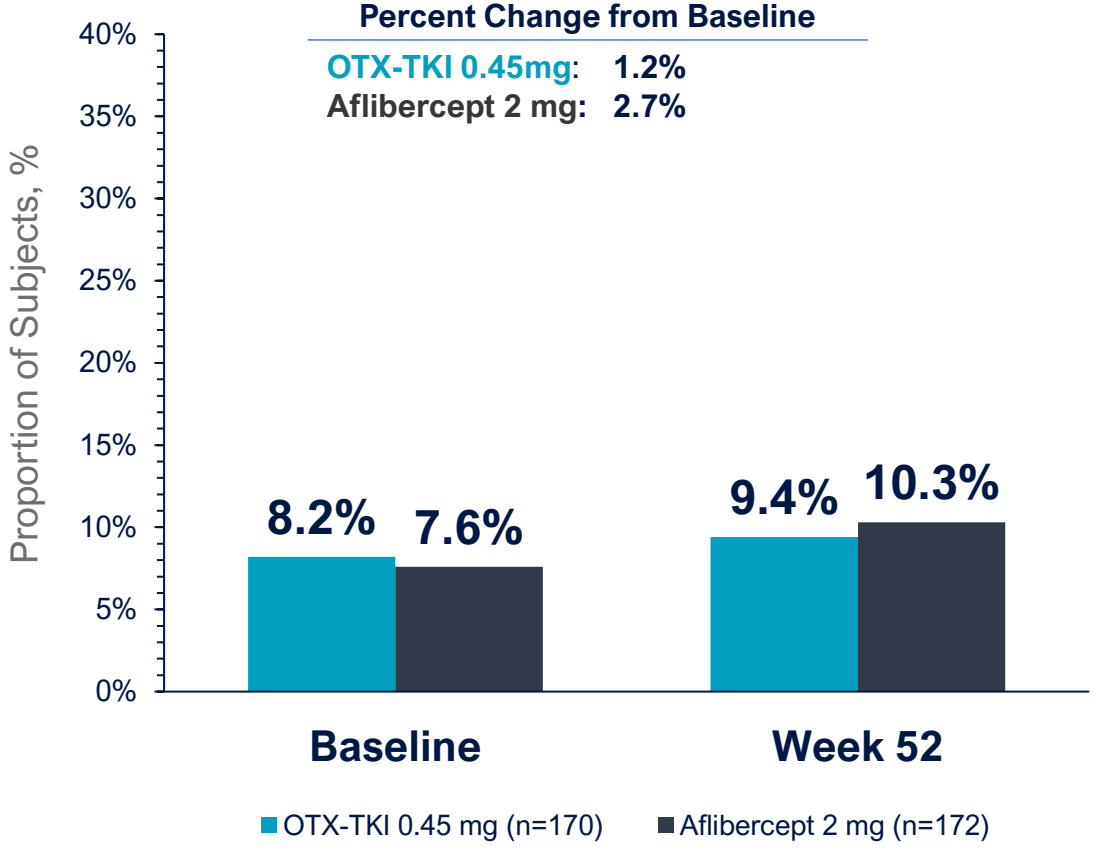
OCULAR THERAPEUTIX Retina experience redefined

*23 events in the study eye, 21 subjects; No case observed to be associated with cataract formation
Optos images on day of onset of AE of vitreous floaters
OTK-TKI: Mean change from baseline (SD) in BCVA, -3.3 (8.2) ETDRS letters; median change from baseline, -1.0 ETDRS letters
Study is ongoing until Year 2
SD, standard deviation; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; AE, adverse events; IOI, intraocular inflammation

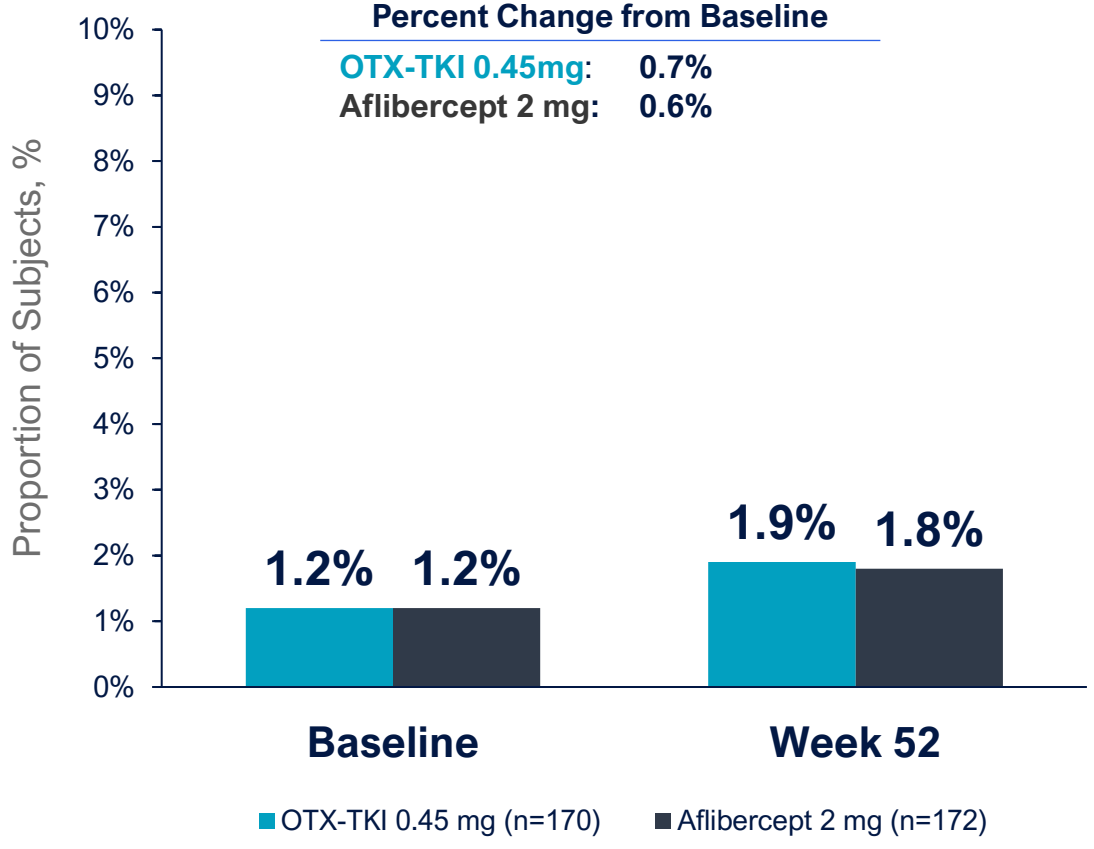
Incidence of Macular Atrophy in SOL-1

Safety Analysis

Any Macular Atrophy[1]



Macular Atrophy in the Central 1mm[1]



[1]cRORA measured by the reading center

cRORA, complete retinal pigment epithelium and outer retinal atrophy

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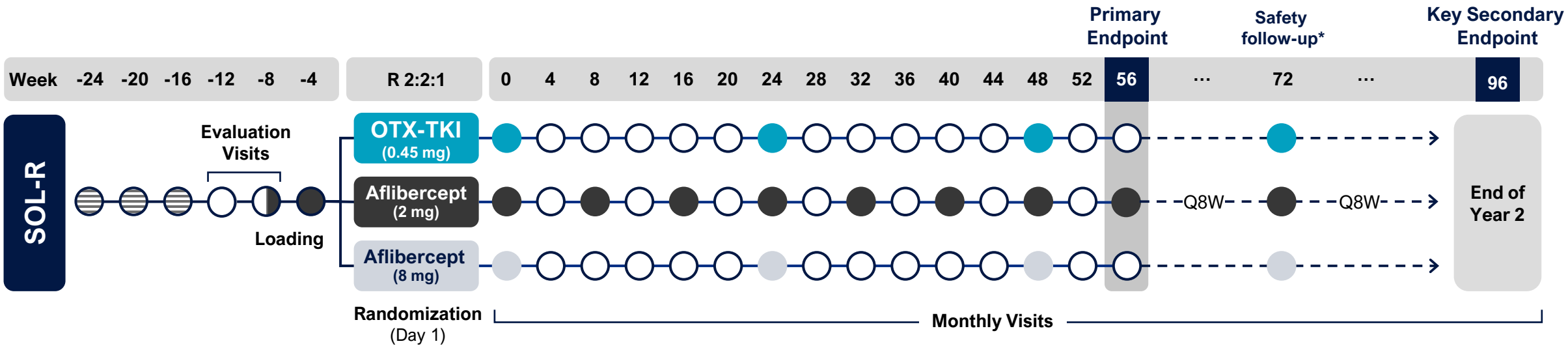
nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

SOL-R: Evaluation of with OTX-TKI relative to aflibercept 2 mg and 8 mg



Aflibercept 8mg dosing identical with no sham injections

Primary analysis:

OTX-TKI dosed Q24W vs. aflibercept 2mg Q8W

Key Secondary Endpoint:

Superiority comparison at Year 2 vs. aflibercept 8mg

Secondary Endpoint:

Evaluating prevention of fibrosis & atrophy vs. aflibercept 2mg

Screening Dose, Any Anti VEGF* | 2nd evaluation & Aflibercept 2mg | OTX-TKI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

*Any anti-VEGF except Beovu
ClinicalTrials.gov identifier: NCT06495918
Q24W, every 24 weeks; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor; † Any anti-VEGF except Beovu

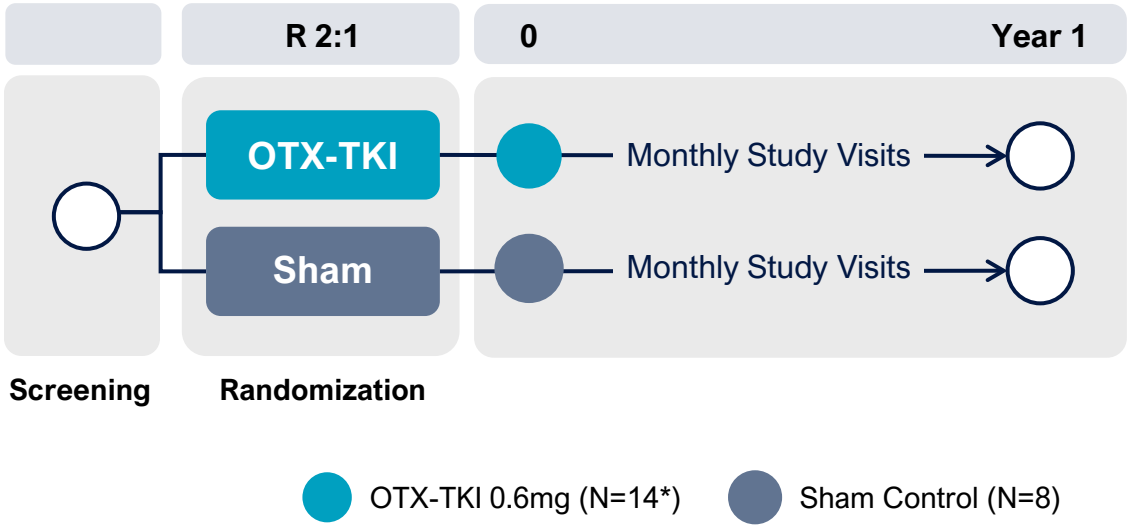
OCULAR THERAPEUTIX Retina experience redefined

HELIOS-1 Study of OTX-TKI in NPDR

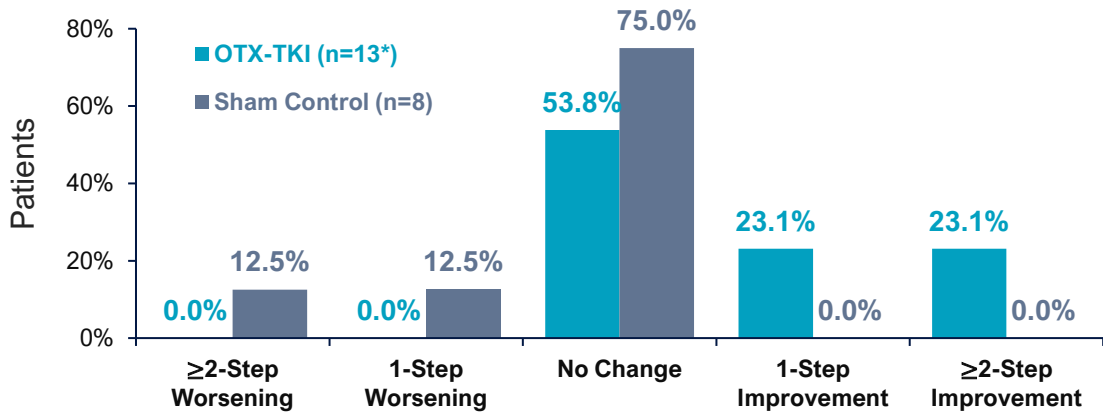
HELIOS-1

Design

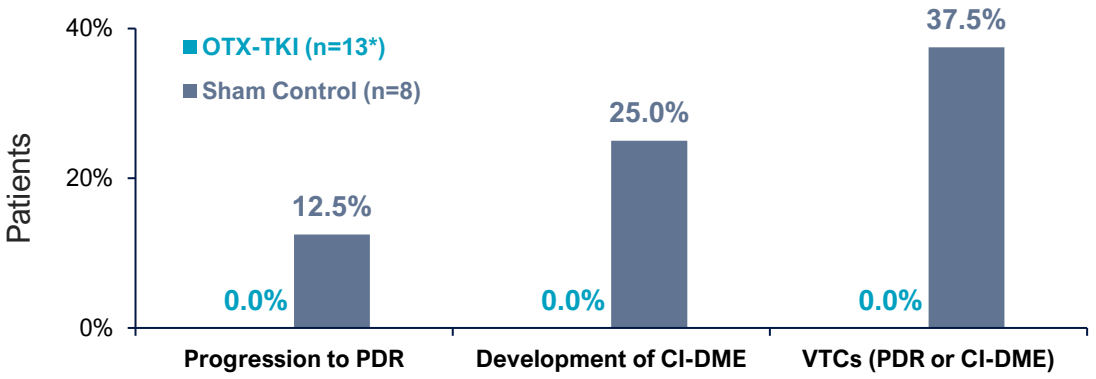
Multi-center, double-masked, randomized, parallel group study of OTX-TKI in moderately-severe to severe NPDR without CI-DME



Change in DRSS from Baseline to Week 48[1]



Progression to VTCs at Week 48[2]



OCULAR THERAPEUTIX Retina experience redefined

*14 subjects enrolled in OTX-TKI treatment arm, with one subject death unrelated to treatment.
DRSS, diabetic retinopathy severity scale; NPDR, non-proliferative diabetic retinopathy; CI-DME, center-involved diabetic macular edema; PDR, proliferative diabetic retinopathy; VTC, vision-threatening complication

HELIOS-1: Total Retinal Vascular Leakage

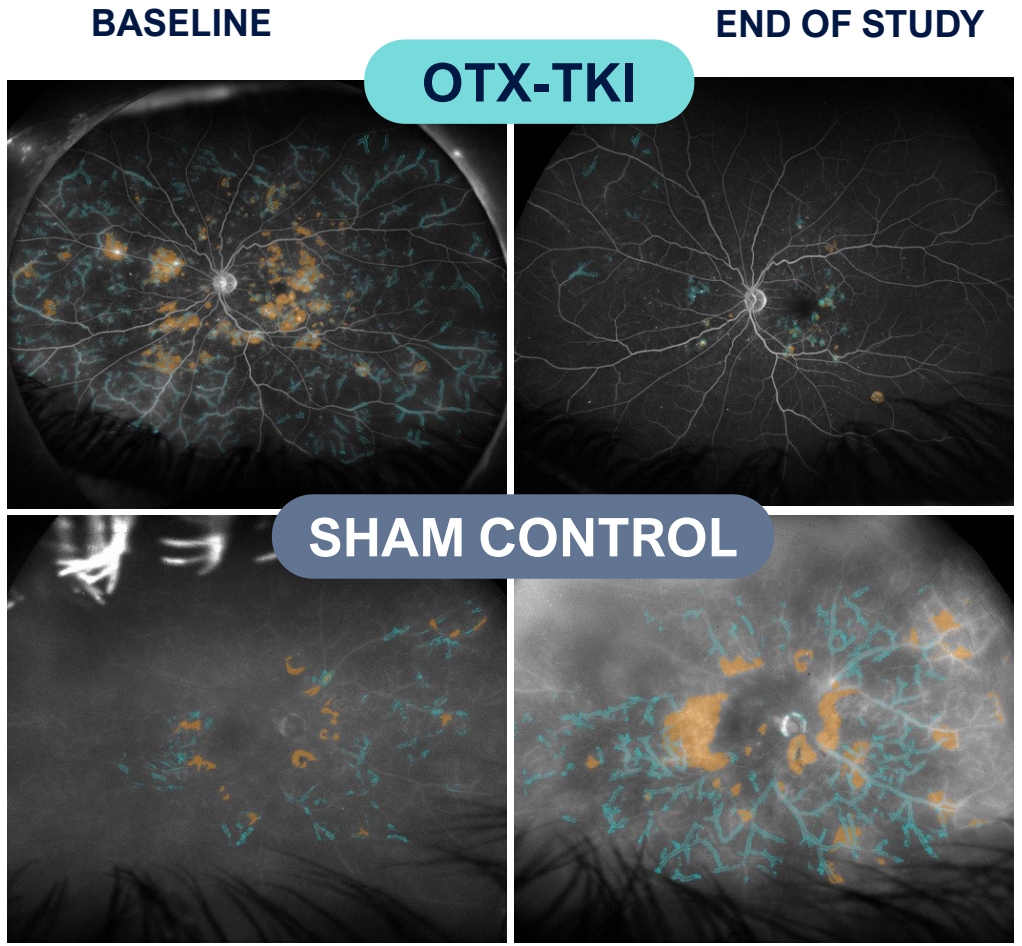
Post Hoc Analysis

HELIOS-1

HELIOS

Higher levels of total retinal vascular leakage associated with[1]:

- More advanced DR
- Greater risk of disease progression
- Worse visual outcomes



Clinical images of ultrawidefield fluorescein angiography (UWF-FA) leakage of one patient. Individual results may vary.

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined

*14 patients enrolled in OTX-TKI treatment arm, with one patient death unrelated to treatment.

1. Ehlers J, et al. *Ophthalmol Retina.* 2025;9(3):243-252. 2. Figures from Ehlers J, et al. Volumetric Macular Fluid Analysis of the Impact of a Single Axitinib Intravitreal Implant (OTX-TKI) from the HELIOS Clinical Trial for Diabetic Retinopathy. Presented at Angiogenesis. Virtual. February 8, 2025.

DR, diabetic retinopathy

Diabetic Retinopathy Program

HELIOS-3 Study Design

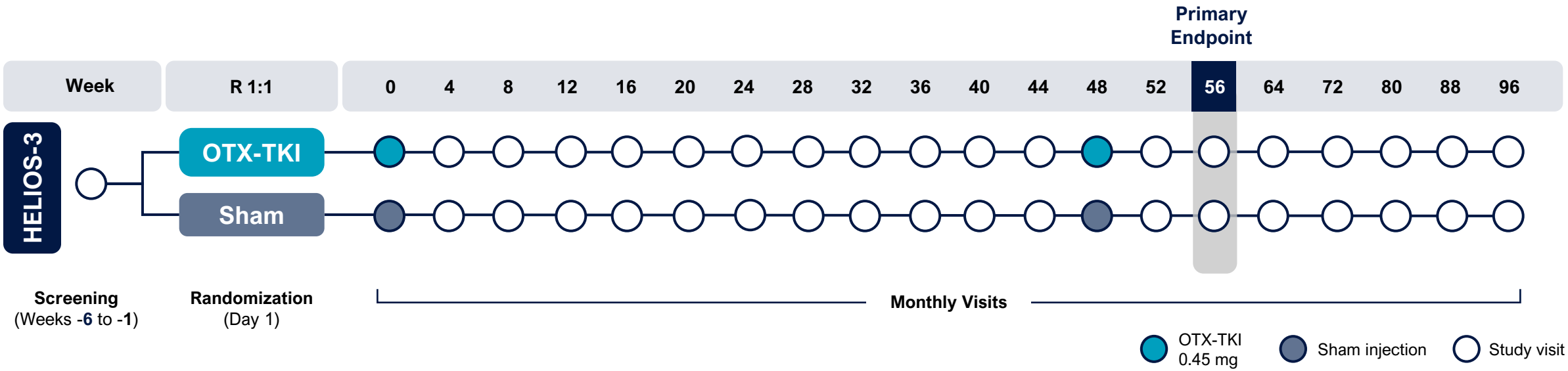
Evaluation of only Q12M OTX-TKI regimen vs Sham

Design

Superiority study of OTX-TKI in **~620** subjects with moderately-severe to severe NPDR without CI-DME

Primary Endpoint (Week 56)

Ordinal DRSS 2-step change status at **Week 56** from baseline
(≥ 2 step improvement, ≥ 2-step worsening, < 2-step change in either direction)



OCULAR THERAPEUTIX Retina experience redefined

ClinicalTrials.gov Identifier: NCT07235085

CI-DME, center involved diabetic macular edema; DR, diabetic retinopathy; NPDR, non-proliferative DR; DRSS, Diabetic Retinopathy Severity Score; Q12M, every 12 months

SOL-1 Results Demonstrate Potential Treatment Benefit of OTX-TKI

SOL-1

Superiority Primary Endpoint Successfully Met

OTX-TKI Demonstrated Superior Maintenance of Vision Compared to Aflibercept 2mg at Week 36*

First trial to demonstrate durability ≥ 9 months

In a post hoc analysis, 74.7% of subjects treated with OTX-TKI did not receive rescue treatments by Week 36

Unmatched Durability

Visual and anatomic stability with OTX-TKI

In a post hoc analysis, OTX-TKI subjects maintained visual and anatomical outcomes, with most remaining rescue-free through Week 36

Sustained Disease Control

OTX-TKI demonstrated a well-tolerated safety profile through Week 52

There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis

Well-Tolerated

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline
Rescue-free subjects include those who did not require rescue injections as specified by the protocol